EAST WEST UNIVERSITY

# IMPACT OF CALCIUM AND VITAMIN-D SUPPLEMENT ON THE DISSOLUTION PROFILE OF ROPITOR®

A Dissertation submitted to the East West University, Bangladesh,

For the partial fulfillment of the Degree of
Bachelor of Pharmacy


**Submitted by**

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# DECLARATION

The research work entitled "Impact of Calcium & Vitamin D Supplement on the Dissolution Profile of Ropitor®" is submitted as a dissertation for the partial fulfillment of the Bachelor Degree of Pharmacy, under the supervision and guidance of **Md. Anisur Rahman**, Assistant Professor, Department of Pharmacy, East West University, Dhaka**.**

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# Certificate by the Supervisor

This is to certify that the thesis entitled "In-vitro comparative dissolution study of different brands of Ranitidine hydrochloride tablets available in Bangladesh" submitted to the Department of Pharmacy, East West University for the partial fulfillment of the requirement for the award of the degree Bachelor of Pharmacy, is a original record and genuine research work carried out by **Tasnim Kabir Taki, ID: 2013-1-70-021** in 2016 of his research in the Department of Pharmacy, East West University, under my supervision and guidance.

Md. Anisur Rahman
Assistant Professor
Department of Pharmacy
East West University

# Certificate by the Chairperson

This is to certify that the thesis entitled "Impact of Calvimax-D on the Dissolution Profile of Rocovus®", submitted to the Department of Pharmacy, East west University for the partial fulfillment of the requirement for the award of the degree Bachelor of Pharmacy, is a original record and genuine research work carried out by **Tasnim Kabir Taki, ID: 2013-1-70-021** in 2016.

Dr. Shamsun Nahar Khan
Associate Professor & Chairperson
Department of Pharmacy
East West University,Bangladesh

# Dedicated to

My Parents
&
Honorable Teachers

# ACKNOWLEDGEMENT

All praises to thealmighty “ALLAH” for the strengths and blessings given to me in completing this research.

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Tasnim Kabir Taki

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# Abstract

The objective of the research work was to investigate the impact of Calvimax-D® (Calcium supplement tablet), on the dissolution of Rosuvastatin (Ropitor®). During research, we took the Ropitor® as main which is a patent product of Rosuvastatin manufactured by Opsonin Pharmaceutical Ltd and Calvimax-D which is apatent product of Incepta Pharmaceutical Ltd .

My project was to determine the impact of calcium and Vitamin D supplement on the dissolution profile of Ropitor. To finding out the target , we performed some essential in vitro test such as dissolution test, dissolution of Ropitor individually and in combination with Calvimax-D.

The physical parameters of Ranitidine tablets were determined by performing weight variation test, hardness test and thickness test. The dissolution test was performed by using distilled water (used asdissolution medium) with USP dissolution apparatus II followed by UV Spectroscopy.A standard curve equation of Rosuvastatin was established for the calculation of percent dissolved amount of drug. The dissolution of individual Rosuvastatin( Ropitor®) tablets and also in combination with the calcium supplement drug Calvimax-D® ( Calcium and Vitamin D) were determined after 10, 20, 30,40 , 50 and 60 minutes. After an hour, the percent release of individual Ropitor® was found between 46.05 % to 71.46% and the percent release of Ropitor® with Calvimax-D® were between 38.08% to 61.01%. After that the impact of supplement drug on the dissolution of Ropitor had been determined.

From the result it was assummed that if the dissolution of Ropitor is affected due to the impactof Calvimax-D (Calcium and Vitamin D) then we should avoide administration of that supplement drug with Ropitor.



**Keyword: UV Spectroscopy, USP dissolution apparatus II, Hardness, Thickness, Weight Variation, Dissolution Impact**

# CHAPTER ONE

# Introduction

Due to the convenience and ease of drug delivery the oral route of drug administration is mostly preferred. Swallowing drug is also familiar and comfortable to patients if they are given the dosage form in oral route. There are a number of reasons for which mode of drug delivery can be inefficient and problematic. When a drug is administered orally then a common problem that hampers the bioavailability of drug is its poor drug absorption. (Ramu et al., 2013)

A drug needs to undergo dissolution before going to the gastrointestinal site for absorption. If the drug is not dissolved in the gastrointestinal fluid then it may lead to poor drug bioavailability. Again if the drug is co-administered with other drug then also the absorption may be hampered (Swati et al., 2013).

This research project was done to observe the impact of calcium and vitamin D supplement when they are co-administered with rosuvastatin drug. Rosuvastatin is a lipid lowering drug that is prescribed in several disease conditions and to reduce the risk of cardiovascular diseases. Calcium and vitamin D supplement are also prescribed to prevent osteoporosis and for many other conditions.

In this research project Ropitor®(Rosuvastatin) from Incepta Pharmaceuticals and Calvimax-D (Calcium and Vitamin D) from Incepta pharmaceuticals were taken. The strength of Ropitor® was 10 mg and the strength of Calvimax-D was 500 mg. The impact of drug dissolution as both individual and in combination with supplement was observed for 60 minutes. Samples were collected as an interval of 10 minutes. Then the absorbance of the sample was measured in the UV spectrophotometer at a wavelength of 241 nm and the percent of drug release was finally calculated.

## 1.2.Cholesterol

Cholesterol is a waxy , fat like substance that is found in all cells of the body. Body needs some cholesterol to make hormones, vitamin D, and substances that helps to digest food that we eat. Cholesterol travels through the bloodstream in small packages called lipoprotein.Two kinds of lipoproteins carry cholesterol throughout the body ; low-density lipoproteins (LDL) and high-density lipoproteins (HDL). Having healthy level of both types of lipoproteins is important. LDL cholesterol sometimes is called “bad” cholesterol because a high LDL level leads to a buildup of cholesterol in the arteries.HDL cholesterol sometimes is called “good” cholesterol because it carries cholesterol from other parts of the body back to the liver.

( National Institute of Health, 2016)

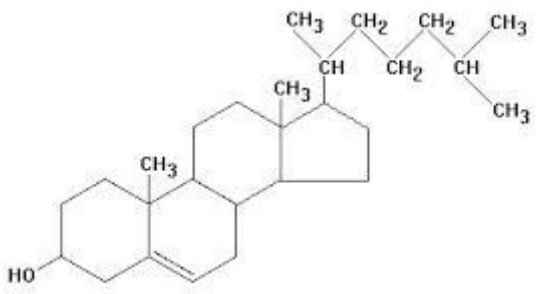


Figure 1.1.: Molecular Structure of Cholesterol(medicine net, 2015)

## 1.3.High Blood Cholesterol

High blood cholesterol is a condition in which a person has too much cholesterol in his blood. By itself the condition usually has no sign and symptoms. Thus, many people don’t know that their cholesterol level is too high.People who have high blood cholesterol have a greater chance of coronary heart disease, also called coronary artery disease.The higher the level of LDL in the blood the greater the chance of getting heart disease. The higher the level of HDL cholesterol in the blood the lower the chance of getting heart disease. High level of LDL leads to

atherorosclerosis ( a disease in which plaque builds up inside the coronary arteries where the plaque is made of cholesterol, fat , calcium and other substance found in the blood).

(National Institute of Health, 2012)

## 1.4.Disease Linked to High Cholesterol

- Coronary heart disease
- Stroke
- Peripheral Vascular disease
- Type II Diabetes
- High blood pressure
- Atherosclerosis ( Cleveland Clinic, 2013)

## 1.5.Drugs to treat high cholesterol

### Table 1.1. Drugs to treat high cholesterol

| Drug class | Drug names | Benefits | Side effects |
|---|---|---|---|
| Statin | Rasuvastatin, Atorvastatin Lovastatin etc. | Decrease LDL and triglycerides, slightly increase HDL | Constipation, nausea,diarrhea, stomach pain, cramps, muscle soreness, pain and weakness |
| **Niacin** | Niaspan, Niacor | Decreases LDL and triglycerides, increases HDL | Facial and neck flushing, nausea, gout, vomiting, diarrhea, high blood sugar, peptic ulcers, itching |
| **Fibrates** | Antara, Tricor | Decrease LDL and triglycerides, increase HDL | Nausea, stomach pain |

| | | | |
|---|---|---|---|
| **Omega-3 fatty acids** | Lovaza, Vascepa | Decrease triglycerides; may increase HDL | Belching, fishy taste, indigestion |
| **Bile acid binding resins** | Colestid, Prevalite,Welchol | Decrease LDL | Constipation, bloating, nausea, gas |

(Mayo Clinic ,2016)

### 1.5.1.General information of Statin

"Statins" is a class of drugs which lowers the level of cholesterol in the blood by reducing the production of cholesterol by the liver. The other source of cholesterol in the blood is dietary cholesterol. Statins block the enzyme in the liver that is responsible for making cholesterol. This enzyme is called Hydroxy-Methylglutaryl-Coenzyme which is a reductase (HMG-CoA reductase).Scientifically, statins are referred to as HMG-CoA reductase inhibitors.

(Medicinenet,2016)

### 1.5.2.Use of Statins

Statin is used for preventing and treating atherosclerosis that causes chest pain, heart attack, strokes in individuals who have or are at risk for atherosclerosis. Most individuals are placed on statin because of high level of cholesterol. The goal of treatment with statin is not only the reduction of cholesterol to normal levels but also the prevention of the complications of atherosclerosis like angina, heart attacks, stroke and death.

(Medicinenet,2016)

### 1.5.3.Side effect of Statin:

The most common side effect of statins are:

- headache
- nausea
- vomiting

- constipation
- diarrhea
- rash
- weakness and
- muscle pain

The most serious side effects are liver failure and rhabdomyolysis ( injury or death of muscle tissue).

(Medicinenet , 2016)

### 1.5.4.Examples of Statins

- Atorvastatin
- Fluvastatin
- Lovastatin
- Pravastatin
- Rosuvastatin
- Simvastatin and
- Pitavastatin ( Medicinenet, 2016)

## 1.6.Calcium

Calcium is a mineral that is an important part of bones and teeth. The heart, nerves, and blood-clotting systems also need calcium to work. Calcium-rich foods include milk and dairy products, kale and broccoli, as well as the calcium-enriched citrus juices, mineral water, canned fish with bones, and soy products processed with calcium.

(WebMD,2016)

### 1.6.1.Use

Calcium is used for treatment and prevention of low calcium levels and resulting bone conditions including

- osteoporosis (weak bones due to low bone density),
- rickets (a condition in children involving softening of the bones), and
- osteomalacia (a softening of bones involving pain).

Calcium is also used for

- premenstrual syndrome (PMS)
- leg cramps in pregnancy
- high blood pressure in pregnancy (pre-eclampsia) and
- reducing the rate of colon and rectal cancer

Some people use calcium for complications after intestinal bypass surgery, high blood pressure , high cholesterol, Lyme disease to reduce high fluoride levels in children, and to reduce high lead levels.Calcium carbonate is used as an antacid for "heartburn." Calcium carbonate and calcium acetate are also used for reducing phosphate levels in people with kidney disease.

(WebMD, 2016)

### 1.6.2.Mechanism of action of Calcium

Calcium is very essential element for human body.The bones and teeth contain over 99% of the calcium in the human body. Calcium is also found in the , muscles, blood, and other tissue. Calcium in the bones can be used as a reserve that can be released into the body as needed. The concentration of calcium in the body tends to decline as we age because it is released from the body through sweat, skin cells, and waste. In addition, as women age, absorption of calcium tends to decline due to reduced estrogen levels. Calcium absorption can vary depending on race, gender, and age.Bones are always breaking down and rebuilding, and calcium is needed for this process. Taking extra calcium helps the bones rebuild properly and stay strong. (WebMD, 2016)

### 1.6.3.Effectiveness of Calcium

Calcium is effective for :

- Indigestion
- Hyperkalemia ( High levels of potassium in the blood)
- Hypocalcemia (Low levels of calcium in the blood)
- Kidney failure
- Osteoporosis caused by corticosteroid drugs
- Hyperparathyroidism (Parathyroid gland disorder

(WebMD, 2016)

### 1.6.4.Drug interection

Calcium interects with the following drugs

- Quinolone antibiotics
- Tetracycline antibiotics
- Bisphosphonates
- Calcipotriene (Dovonex)
- Diltiazem (Cardizem, Dilacor, Tiazac)
- Digoxin (Lanoxin)
- Levothyroxine
- Verapamil (Calan, Covera, Isoptin, Verelan)
- Water pills (Thiazide diuretics)

( WebMD, 2016)

## 1.7.Vitamin D

Vitamin D is one kind of vitamin. It is found in small amounts in a few foods, including fatty fish such as herring, mackerel, sardines and tuna. To make vitamin D more available, it is added to dairy products, juices, and cereals. But most vitamin D which is 80% to 90% of what the body gets is obtained through exposure to sunlight. Vitamin D can also be made in the laboratory as medicine.

(WebMD, 2016)

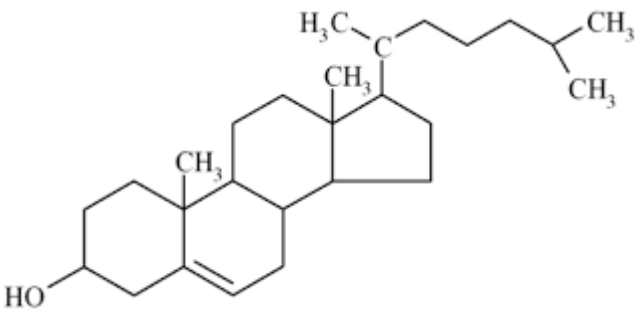


Figure 1.2.: Moleculer structure of Vitamin D (WebMD, 2016)

## 1.7.1.Use of Vitamin D

Vitamin D is used for preventing and treating rickets( a disease that is caused by not having enough vitamin D) which is caused for vitamin D deficiency. Vitamin D is also used for treating weak bones (osteoporosis), bone pain (osteomalacia), bone loss in people with a condition called hyperparathyroidism, and an inherited disease (osteogenesis imperfect) in which the bones are especially brittle and easily broken. It is also used for preventing falls and fractures in people at risk for osteoporosis. It prevents low calcium and bone loss (renal osteodystrophy) in people with kidney failure. Vitamin D is used for conditions of the heart and blood vessels, including high blood pressure and high cholesterol. It is also used for diabetes, obesity, muscle weakness, multiple sclerosis, rheumatoid arthritis, chronic obstructive pulmonary disease (COPD), asthma, bronchitis, premenstrual syndrome (PMS), and tooth and gum disease.Some people use vitamin D for skin conditions including vitiligo, scleroderma, psoriasis, actinic keratosis, and lupus vulgaris.It is also used for boosting the immune system, preventing autoimmune diseases, and preventing cancer.

(WebMD, 2016)

## 1.7.2.Mechanism of action

Vitamin D is necessary for the regulation of the minerals calcium and phosphorus found in the body. It also plays an vital role in maintaining proper bone structure.Sun exposure is an easy and

reliable way for most people to get vitamin D. Exposure of the face, hands, arms, and legs to sunlight two to three times a week for about one-fourth of the time it would take to develop a mild sunburn will cause the skin to produce enough vitamin D. The necessary exposure time varies with skin type, age, season, time of day, etc.

(WebMD, 2016)

### 1.7.3.Precautions & Warnings

Precautions should be taken for the following conditions

- Pregnancy and breast feeding
- Kidney disease
- High levels of calcium in the blood
- Hardening of the arteries (atherosclerosis)
- Sarcoidosis
- Histoplasmosis
- Over-active parathyroid gland (hyperparathyroidism)
- Lymphoma
- Tuberculosis

(WebMD, 2016)

### 1.7.4.Rosuvastatin

Rosuvastatin is in a group of drugs called "statins." Rosuvastatin reduces levels of "bad" cholesterol (low-density lipoprotein, or LDL) and triglycerides in the blood, while increasing levels of "good" cholesterol (high-density lipoprotein, or HDL). Rosuvastatin is used to lower cholesterol and triglycerides in the blood. Rosuvastatin is also used to lower the risk of stroke, heart attack, and other heart complications in people with diabetes, coronary heart disease, or other risk factors Rosuvastatin is used in adults and children who are at least 10 years old. (medicine health, 2016)

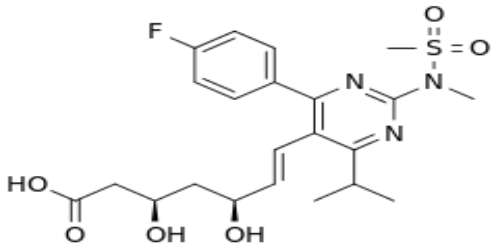


Figure 1.3.:Moleculer structure of Rasuvastatin(medicine health, 2016)

## 1.7.5.Mechanism Of Action

Rasuvastatin is a selective and competitive inhibitor of HMG-CoA reductase, the rate-limiting enzyme that converts 3-hydroxy3methylglutaryl coenzyme A to mevalonate, a precursor of cholesterol. *In vivo* studies in animals, and *in vitro* studies in cultured animal and human cells have shown rosuvastatin to have a high uptake into, and selectivity for, action in the liver, the target organ for cholesterol lowering.

In *in vivo* and *in vitro* studies, rosuvastatin produces its lipid-modifying effects in two ways. First, it increases the number of hepatic LDL receptors on the cell-surface to enhance uptake and catabolism of LDL. Second, rosuvastatin inhibits hepatic synthesis of VLDL, which reduces the total number of VLDL and LDL particles. (RxList Inc,2016)

### 1.7.6.Composition:

**10 mg tablet:** Each tablet contains 10mg rasuvastatin as rasuvastatin calcium

( Drug bank, 2016)

### 1.7.7.Side effects

Rosuvastatin may cause the following side effects

- constipation
- stomach pain
- dizziness
- difficulty falling asleep or staying asleep

- depression
- joint pain
- headache
- memory loss or forgetfulness
- confusion

Some side effects can be serious such as:

- muscle pain, tenderness, or weakness
- lack of energy, fever , chest pain
- yellowing of the skin or eyes, dark colored urine
- pain in the upper right part of the abdomen
- difficulty breathing or swallowing, nausea
- swelling of the face, throat, tongue, lips, eyes, hands, feet, ankles, or lower legs

(medicine plus,2016)

### 1.7.8.Drug interection

Rosuvastatin must not be taken while pregnant as it can cause serious harm to the unborn baby. In the case of breastfeeding, it is unknown whether Rosuvastatin is passed through breastmilk, because of the potential of disrupting the infant's lipid metabolism, patients should not breast feed while on rosuvastatin. Colchicine, cyclosporine, daptomycin, fibrates (eg, clofibrate, fenofibrate, gemfibrozil), HIV protease inhibitors (eg, atazanavir, lopinavir, ritonavir), or niacin because they may increase the risk of muscle or kidney problems

- It is also contraindicated to Dronedarone, eltrombopag, or itraconazole because they may increase the risk of rosuvastatin's side effects
- Anticoagulants (eg, warfarin), cimetidine, ketoconazole, sirolimus, spironolactone, or tacrolimus because the risk of their side effects may be increased by rosuvastatin.

- Another statin medicine such as Atorvastatin ,lovastatin,simvastatin
- Antifungal medicine – fluconazole, ketoconazole.

(Drugs.com , 2016)

## 1.7.9.Pharmacodynamics:

Rasuvastatin is a synthetic , enantiomerically pure antilipemic agent. It is used to lower total cholesterol low density lipoprotein-cholesterol (LDL-C), apolipoprotein B (apoB), non-high density lipoprotein-cholesterol (non-HDL-C), and trigleride (TG) plasma concentrations while increasing HDL-C concentrations. High LDL-C, low HDL-C and high TG concentrations in the plasma are associated with increased risk of cardiovascular disease and atherosclerosis. By decerssing LDL-C and TG and incressing HDL-C, rasuvastatin reducesthe risk of cardiovascular morbidity and mortality. ( Drugbank, 2016)

## 1.7.10.Pharmacokinetics

**Absorption**

Peak plasma concentrations of rosuvastatin were reached 3 to 5 hours following oral dosing. Both AUC and Cmax increased in approximate proportion to rasuvastatin dose. Bioavailability of rosuvastatin is about 20%. Food has no effect on the AUC of rasuvastatin

**Distribution**

Mean volume of distribution at steady-state of rosuvastatin is approximately 134 liters. Rosuvastatin is 88% bound to plasma proteins which is mostly albumin. This binding is reversible and independent of plasma concentrations.

**Metabolism**

Rosuvastatin is not extensively metabolized.Approximately 10% of dose is recovered as metabolite. The major metabolite is N-desmethyl rosuvastatin. cytochrome P450 \ 2C9 is primarily responsible for the formulation of rasuvastatins major metabolite , N-desmethylrosuvastatin. N-desmethylrosuvastatin has approximately 50% of the pharmacological activity of its parent compound in vitro. Rasuvastatin clearance is not dependent on metabolism

by cytochrome P450 3AA to a clinically significant extant. Overall, greater than 90% of active plasma HMG CoA reductase inhibitory activity is accounted for by the parent compound.

**Excretion**

Rasuvastatin is administrated orally and its metabolites are primarily excreted in the feces (90%). The elimination half-life (t½) of rosuvastatin is approximately 19 hours.After an intravenous dose, approximately 28% of total body clearance was via the renal route, and 72% by the hepatic route. (Rxlist,2016)

## 1.7.11.Storage

Keep this medication in the container it came in, tightly closed, and out of reach of children. Store it at room temperature and away from excess heat and moisture (not in the bathroom).

(Medicine plus, 2016)

### 1.7.12.Missed dose

Take the missed dose as soon as you remember it. However, if it is less than 12 hours before your next dose is scheduled, skip the missed dose and continue your regular dosing schedule. Do not take a double dose to make up for a missed one. (Medicine plus, 2016)

## 1.7.13.Overdose

There is no treatment for overdose.in case of overdose, the patient should be treated symptomatically and supportive measures should be taken as required. Hemodialysis does not significantly enhance clearance of rasuvastatin. (rxlist,2016)

## 1.7.14. Contraindication

Rasuvastatin is contraindicated in the following conditions:

- Patients with a known hypersensitivity to any component of this product. Hypersensitivity reactions including rash, pruritus, urticaria, and angioedema have been reported with Rasuvastatin
- Patients with active liver disease, which may include unexplained persistent elevations of hepatic transaminase levels.
- During pregnancy .
- Lactation. Limited data indicate that Rasuvastatin is present in human milk as statins have the potential for serious adverse reactions in nursing infants. Women who require Rasuvastatin treatment should not breastfeed their infants. ( rxlist ,2016)

## 1.7.15.Indications

- Hyperlipidemia And Mixed Dyslipidemia
- Pediartric patients with familial Hypercholesterolemia
- Hypertriglyceridemia
- Primary dysbetalipoproteinemia ( Type II Hyperlipoproteinemia)
- Adult patients with homozygousfamilial hypercholesterolemia
- Atherosclerosis
- Atherosclerotic cardiovascular disease
- Cardiovascular disease
- Mixed dyslipidemias
- Primary Hyperlipidemia (rxlist, 2016)

## 1.8.ROPITOR®

### 1.8.1.Description:

Rapitor® is a selective and competitive inhibitor of HMG-CoA reductase , the rate- limiting enzyme that converts 3 –hydroxy-3-methylglutaryl coenzyme A to mevolonate , a precursor of cholesterol.

(Opsonin Pharma ,2016)


Figure 1.4. : Ropitor® 10 mg tablet(Opsonin Pharma ,2016)

### 1.8.2.Mode of action:

Rapitor® is a selective and competitive inhibitor of HMG-CoA reductase , having a mechanism of action similar to that of other statins. Its approximate elimination 19 hours its time to peak plasma concentration is reached in 3-5 hours following oral administration.

( Opsonin Pharma ,2016)

### 1.8.3.Pharmacokinetics

**Absorbtion:** Peak plasma concentration of rosuvastation were reached 3 to 5 hours following oral dosing. Both peak concentration (Cmax) and area under the plasma concentration- time curve (AUC) increased in approximate proportion to Rasuvastatin dose.

**Distribution**

Mean volume of distribution at steady-state of Rosuvastatin is approximately 134 liters. Rosuvastatin is 88% bound to plasma proteins which is mostly albumin. This binding is reversible and independent of plasma concentrations.

**Metabolism:** Rosuvastatin is not extensively metabolized. Approximately 10% of dose is recovered as metabolite. The major metabolite is N-desmethyl rosuvastatin. cytochrome P450 \ 2C9 is primarily responsible for the formulation of rasuvastatins major metabolite which is N-desmethylrosuvastatin. N-desmethylrosuvastatin has approximately 50% of the pharmacological activity of its parent compound in vitro. Here , greater than 90% of active plasma HMG CoA reductase inhibitory activity is accounted for by the parent compound.

**Ellimination:** Raosuvastatin is administrated orally and its metabolites are primarily excreted in the feces (90%). The elimination half-life (t½) of Rosuvastatin is approximately 19 hours. Approximately 28% of total body clearance was via the renal route, after an intravenous dose and 72% by the hepatic route. ( Opsonin Pharma ,2016)

## 1.8.4.Composition

**Rapitor® 5 mg Tablet:** Each film coated tablet contains Rosuvastatin 5 mg as Rasuvastatin calcium INN.

**Rapitor® 10 mg Tablet:** Each film coated tablet contains Rosuvastatin 10 mg as Rasuvastatin calcium INN.

**Rapitor® 20 mg Tablet:** Each film coated tablet contains Rosuvastatin 20 mg as Rasuvastatin calcium INN. (Opsonin Pharma ,2016)

### 1.8.5.Indications:

- Primary hypercholesterolemia
- Heterozygous Hypercholesterolemia
- Homozygous Hyper holesterolemia
- Coronary heart disease

(Opsonin Pharma ,2016)

### 1.8.6.Dosage & administration

Primary hypercholesterolemia, Heterozygous Hypercholesterolemia and Mixed Dyslipidemia :

The usual recommended starting dose of Rosuvastatin is 10 mg once daily.

(Opsonin Pharma ,2016)

### 1.8.7.Contraindication

- Rasuvastatin is contraindicated in patient with a known hypersensitivity to any component of this product.
- Rasuvastatin is contraindicated in patient with active liver disease.

(Opsonin Pharma ,2016)

### 1.8.8.Side effects

Rasuvastatin is generally well tolerated. The side effects are

- Myalgia
- Constipation
- Asthenia
- Abdominal pain
- Nausea (Opsonin Pharma ,2016)

## 1.8.9.Precautions

Caution should be taken in patients with thyroid problem , have family history of mascular disorder and if had any past problrms with muscles . (Opsonin Pharma ,2016)

## 1.8.10.Overdose

If there is incident like overdose , the patient should be treated symptomatically , and supportive measures instituted as required. (Opsonin Pharma ,2016)

## 1.8.11.Storage

Rapitor® should be stored in a cool and dry place which is protected from light.

(Opsonin Pharma ,2016)

## 1.8.11.Commercial Packaging

**Rapitor® 5 mg Tablet:** Each cartoon contains 10 x 3 tablets in Alu-Alu blister pack
**Rapitor® 10 mg Tablet:** Each cartoon contains 10 x 2 tablets in Alu-Alu blister pack
**Rapitor® 20 mg Tablet:** Each cartoon contains 10 x 1 tablets in Alu-Alu blister pack

(Opsonin Pharma ,2016)

## 1.9.Calcimax

### 1.9.1.Description

Calcium is an important element and plays vital role in our body. It helpd body's framework stronger by building bone. Clinical evidence suggest that calcium is useful for prevention and treatment of osteoporosis and associated fractures. Vitamin-D is also essential fof healthy bones as it aids in calcium absorbtion from the GI tract. ( Incepta pharmaceutical ,2016)


Figure: Calvimax D Tablet (Incepta pharmaceutical)

### 1.9.2.Composition

Calvimax Tablet: Each tablet contains Calcium Carbonate 1250 mg equivalent to 500 mg of elemental Calcium and Cholecalciferol 200IU equivalent to 5µ vitamin D3.

( incepta pharmaceutical , 2016)

### 1.9.3.Indications

- Treatment of osteoporosis , reckets, osteomalacia,
- In pregnancy and lactation due to increase demand
- In kidney disease andpancreatitia
- During therapy with antiseizure medication
- The prevention and treatment of calcium deficiency , vitamin D deficiency

( incepta pharmaceutical , 2016)

### 1.9.4.Dosage and administration

Adult and Elderly and children above 12 years of age : 2 tablets per day, preferably one tablet each morning and evening.

Children: Not recommended for children under 12 years

(Incepta pharmaceutical , 2016)

### 1.9.5.Side Effects

Mild gastro-intestinal disturbance such as

- Constipation
- Flatulence
- Nausea
- Gastric pain
- Diarrhea
- Rash
- Hypercalciuria
- Hypercalcemia ( Incepta pharmaceutical , 2016)

## 1.9.6.Precaution

Patients with mild to moderate renal failure or mild hypercalciuria should be supervised with care. Urinary calcium excretion should be measured. Patients with a history of renal stones urinary calcium excretion should be measured to exclude hypercalciurea.

( Incepta pharmaceutical , 2016)

## 1.9.7.Contraindication

Contra-indications of Calvimax® are

- Hypercalcaemia
- Primary hyperparathyroidism
- Vitamin D overdose
- Severe renal failure
- Osteoporosis (Incepta pharmaceutical, 2016)

## 1.9.8.Overdose

The most serious consequence of acute or chronic overdose is hypercalcemia due to vitamin D toxicity. Chronic overdose can lead to vascular and organ calcification as a result of hypercalcemia (Incepta pharmaceutical , 2016)

## 1.9.10.Commercial Packaging

Clavimax tablet: Bottle containing 30 tablet (Incepta pharmaceutical , 2016)

## 1.10.Dissolution

Dissolution is the transfer of molecules of ions form solute state in a solution .It is the process of dissolving solid part (solute) in the solvent (liquid). In more simple way, Dissolution is the process by which a substance turns in to solution in a solvent. For solids, dissolution is explained as the breakdown of the crystal lattice into individual ions, atoms or molecules. Dissolution is a total kinetic process. The result of dissolution is controlled by the thermodynamic energies involved in the process, such as the heat of solution and entropy of
solution, but the dissolution itself is not. Overall the free energy must be negative for net dissolution to occur. In turn, those energies are controlled by the way in which different chemical bond types interact with those in the solvent (Sirius-analytical, 2016).

## 1.10.1.Rate of dissolution

The rate of total dissolution indicates the speed of the total process. Rate of dissolution depends on the chemical natures of the solvent and solute, such as; temperature, the degree of unsaturation, the interfacial surface area and the presence of inhibitors like substances which are absorbed on the surface.

Noyes-Whitney equation or the Nernst and Brunner equation can express the rate of dissolution. The equation is:

$dm/dt = AX \{ D/d \}X( C_s-C_b)$;

where, m= mass of solute material

t= time

A= surface area of interface between the dissolving substance and the solvent

D= diffusion coefficient

d= thickness of the boundary layer of the solvent at the surface of the dissolving substance

$C_s$= mass concentration of the substance on the surface

$C_b$= mass concentration of the substance in the bulk of the solvent

In case of dissolution limited by diffusion, $C_s$ is equal to the solubility of the solute. When the dissolution rate of a pure substance is normalized to the surface area of the solid then it is denoted by $kg/m^2S$ and termed as 'intrinsic dissolution rate'.

(Lentle and Janssen, 2011)

## 1.10.2.Process of dissolution

On the basisof rule, ' like dissolves like'; means that substances must have the same intermolecular forces to form solutions. The particles of solute interact with the particles of solvent after the introduction of a soluble solute into the solvent. In solid or liquid solute, the interactions between the solute particles and the solvent particles are so strong that the individual solute particles separate from each other and surrounded by solvent molecules, traverse to the solution. In the case of water as solvent, the salvation word is replaced by the word hydration. After dissolving a solute, the individual particles of solute become surrounded by solvent particles. Eventually the particle separates from the remaining solute, surrounded by solvent molecules in solution. Moreover, if the solute is ionic, the individual ions get separated from each other and become surrounded by solvent particles. So the ions of solute separate when the solute dissolves. This process is knowns as dissociation. Soluble ionic compounds are often known as electrolytes. Many ionic compounds dissociate completely and they are called strong electrolytes. Sodium salts are example of strong electrolytes. Weak electrolytes are those which are dissolved but get dissociated in partial amount and solutions of such solutes may conduct electricity weakly such as; acetic acid.

( Lapsurgery, 2014)

### 1.10.3.Factors which influence the dissolution of a substancee

- Temperature
- Particle size of solute
- Agitation
- Solvent selection

**Temperature**

In most cases of dissolution of solute in a liquid is based on the absorption of heat. The dissolution will be more rapid, if the temperature is elevated but in lower temperature the dissolution will be less. So, temperature has the important influence on dissolution.

**Particle size**

Particle size also influences the dissolution rate. The more size of particles, the less the rate of dissolution. The absorption depends on the dissolution rate. So the rectification of dissolution rate of any solute is very important.

**Agitation**

Concentration of the solvent also determines the dissolution. The more concentrated the solvent, the less the rate of dissolution.

**Solvent selection**

Dissolution rate also depends upon the type of solvent. In oily solvent dissolution rate is slower than in water. (Yeomans, 2000)

# CHPTER TWO
# Literature Review

Different types of research projects about Statins had done by researchers before I did. Among those research works some of are mentioned below:

In 1998 A study was done to determine if a combination therapy with simvastatin and Urodeoxycholic Acid was more effective for cholesterol sallstone dissolution than was Urodeoxycholic Acid monotherapy.The result of this study showed that combination therapy with simvastatin and ursodeoxycholic acid was more effective for cholesterol gallstones dissolution than ursodeoxycholic acid monotherapy.

( Tazuma & Susumu ,1998)

In 2000, a research was done to develop a second derivative UV spectroscopic method for the determination of simvatatin in the tablet dosage form. This method was done by using UV spectroscopy. According to this study, the result reflected that a second derivative UV spectroscopy method was an excellent alternative to HPLC method for the dissolution and release testing of Simvastatin. (Wang ,2000)

In 2013 An investigation was done to improve the dissolution of poorly soluble drug like Rasuvastatin Calcium where liquisolid compact technique was used and in-vitro release characteristics at different dissolution conditions was observed. Since liquisolid compacts established significantly higher drug release rates so it could be a promising strategy in improving the dissolution of poor water soluble drugs and formulating immediate release solid dosage forms. ( Kapur, 2013)

In 2014 a research shows Rasuvastatin is a poorly water soluble drug and the rate of its oral absorption is controlled by the dissolution rate in the gastrointestinal tract.The tabletting properties of the liquisolid compacts were within the acceptable limits and liquisolid compacts demonstrated significantly higher drug release rates than those of conventional and marketed tablet due to increasing wetting properties and surface area of the drug. So it is a promising alternative for improvement of the dissolution rate of water insoluble drug.

( Ram, 2014)

In the year of 2006, one research was studied to improve the solubility and dissolution rate of a poorly water-soluble drug, Simvastatin by solid dispersion technique. By this study, it was determined that tablets containing solid dispersion prepared with PEG and PVP showed significant improvement in the release profile of Simvastatin as compared to tablet containing Simvastatin without PEG or PVP (Patel , 2006)

At 2008, simvastatin was studied in a research paper to enhance the solubility and dissolution by using hydrophilic, low viscosity grade polymer hydroxypropyl methylcellulose. In this thesis, co solvent evaporation and spray drying method were used. Result from the research showed that the conversion of crystalline form of simvastatin into amorphous.

(Panday, Gattani & Jain ,2008)

In 2007 a study was done to improve the solubility and dissolution rate of a poorly water-soluble drug, Lovastatin, by a solid dispersion technique since it improve the dissolution rate, and hence possibly bioavailability, of a range of hydrophobic drugs.Tablets containing solid dispersion prepared with PEG and PVP showed significant improvement in the release profile Lovastatin compared with tablets containing Lovastatin without PEG or PVP. .

(Patil,2007)

In the year of 2010, a study was done which objective was to formulate surface solid dispersions of simvastatin to improve the aqueous solubility and dissolution rate to facilitate faster onset of action. To accomplish this study, co-evaporation method was used. The result showed that solid dispersion increased dissolution rate of that drug.

(Rao, Mandagi & Thanki ,2010)

In 2011 a review was done on a new, simple, precise, rapid, and accurate reverse phase liquid chromatographic method for formulation containing Rosuvastatin Calcium as active pharmaceutical ingredient.Results proved that this method can be useful in the routine analysis

for the determination, development and to validate a new High Performance Liquid Chromatographic method (HPLC) for such an analysis.

(Kumar, ranjan and Bhusan,2011)

In the year 2011, an investigation was done to increase the solubility and dissolution rate of simvastatin by the preparation of nanosuspensions with Pluronic F127 and zirconium oxide beads. In this study wet-milling technique was applied at the laboratory scale. The result of this investigation showed that the preparation of simvastatin loaded nanosuspensions significantly improved the in vitro dissolution rate, thusly enhancing the fast onset of therapeutic drug effect.

( Pandya and Patel, 2011)

In 2012 a study showed that solid dispersions greatly enhance the surface area.So the dissolution rate and the bioavailability of poorly water-soluble drugs are raised.So the solvent evaporation method is a promising method for formulating uniform and stable lovastatin solid dispersions with enhanced surface area and dissolution rate. The bioavailability also increased for increasing wettability of the solid dispersions.

(Shaikh and Patwekar,2012)

In 2012 a study was done to enhance the dissolution profile, absorption efficiency and bioavailability of water insoluble drugs like Lovastatin by using various techniques. Lovastatin is a poorly soluble, highly permeable drug and the rate of its oral absorption is often controlled by the dissolution rate in the gastrointestinal tract.the results suggest that superdisintegrant method was preferred due to its simplicity, low cost and industrial feasibility.

(Neduri and Kumar,2012)

In the year of 2012, one article was written which objective was to prepare simvastatin nanocrystals to enhance its dissolution rate and bioavailability by using sonoprecipitation method. The result of this study showed that this method could produce small and uniform simvastatin nanocrystals with an improved saturation solubility, dissolution rate and oral bioavailability.

(Jiang, Han & Zhao ,2012)

In the year 2012, a research was done for the improvement of the solubility and dissolution rate of Atorvastatin by Solid Dispersion technique and solvent evaporation method. By using this method, it was found that hydrophilic carrier Poloxamer 188 was found to be played a vital role in the improvement of the dissolution property. (Jahan,Islam & Tanwir ,2012)

In 2012 a review was done to enhance the aqueous solubility of simvastatin by techniques employing solid dispersions, microencapsulation, supercritical fluid and the cyclodextrin inclusion system are described and systematically compared.

(Rubia and Narvo , 2012)

In 2013 An investigation was done to improve the dissolution of poorly soluble drug like Rasuvastatin Calcium where liquisolid compact technique was used and in-vitro release characteristics at different dissolution conditions was observed. Since liquisolid compacts established significantly higher drug release rates so it could be a promising strategy in improving the dissolution of poor water soluble drugs and formulating immediate release solid dosage forms.

( Kapur, 2013)

In 2013 Rosuvastatin calcium face a problem of low bioavailability (absolute bioavailability 20%) for its Poor solubility and permeability of slightly soluble drug. Non-ionic surfactants (Span 20,Span 60,span 80), cholesterol and lecithin in different ratios by film hydration was used in this this study. Niosomal formulations were prepared and all formulas gave obvious morphology in the presence of cholesterol as a stabilizing agent observerd.It is proved that niosoms are promising dosage form for enhance dissolution and permeability of slightly soluble drugs prepared by film hydration method.

( Saleh , 2013)

In 2013 a research was done for the purpose of improving the solubility and dissolution rate of Atorvastatin, a drug belong to the group of statin by Solid Dispersion (SD) technique which was made by physical mixing and solvent evaporation method. Both method used a hydrophilic

carrier Poloxamer 188 which was found to be played a vital role in the improvement of the dissolution property.

( Jahan, Islam and Tanwir ,2013)

At 2013, one study was done which objective was to investigate the effect of polyethylene glycol (PEG) molecular weights as solid dispersion carriers on the dissolution behavior of simvastatin. Here solvent method was used to determine this project. From this preoject result confirmed the influence of PEG molecular weight on drug dissolution rate from solid dispersion systems.

(Bolourchian, Mehdi & Dadashzadeh ,2013)

In 2013 Rosuvastatin is a Dyslipidaemic Agents, which acts by inhibition of HMG-CoA reductase enzyme and used in the treatment of hyperlipidemia. A formulation was designed which is orally disintegrating tablets of Rosuvastatin.It was formulated by Superdisintegrant addition method by direct compression technique.So the formulated tablets of Rosuvastatin containing crosspovidone and sodium starch glycolate are better and effective than conventional tablets to meet patient.

( Rohini , 2013)

In 2014 a research shows Rasuvastatin is a poorly water soluble drug and the rate of its oral absorption is controlled by the dissolution rate in the gastrointestinal tract.The tabletting properties of the liquisolid compacts were within the acceptable limits and liquisolid compacts demonstrated significantly higher drug release rates than those of conventional and marketed tablet due to increasing wetting properties and surface area of the drug. So it is a promising alternative for improvement of the dissolution rate of water insoluble drug.

( Ram, 2014)

In 2014 a research has been done with an objective to prepare a self-emulsifying drug delivery system (SEDDS) of rosuvastatin calcium (ROS) with the least amount of surfactant which could enhance its solubility and oral bioavailability.It was demonstrated that S-SEDDS prepared from liquid SEDDS can be a promising novel approach to enhance the solubility and drug release of ROS.

(Rokad and Nagda , 2014)

In 2014 a study showed that Lovastatin is a poorly soluble, highly permeable drug and the rate of its oral absorption is often controlled by the dissolution rate in the gastrointestinal.The technique of liquisolid compacts is a promising technique towards such a novel aim. liquisolid compacts demonstrated significantly higher drug release rates than those of conventionally made directly compressed tablets.

(Krishna & Kumar, 2014)

In 2014 a study was done for the improvement of the dissolution rate of Atorvastatin Calcium. Solid Dispersion technique was used which was made by modified solvent evaporation method by using modified locust bean gum and it showed outstanding result in the improvement of the dissolution rate of Atorvastatin Calcium. Besides, Co-grinding mixture showed good result in the improvement of the dissolution rate of Atorvastatin Calcium. So, it can be used as an alternative in stead of solid dispersion.

(Panghal & Nagpal, 2014)

In 2014 A research was done to determine the drug-drug interaction between Atorvastatin, Metformin HCL and Multivitamin by doing in vitro dissolution study. Because of drug-drug interaction dissolution rate can varies.Though the dissolution rate of Atorvastatin was less than 50%, but it was far more than the rate of combination. In case of combination they gave antagonistic activity and that's why dissolution rate decrease.

(Islam, 2014)

In 2014 a investigation was done to improve the solubility of the poorly water soluble drug atorvastatin (ATR), using solid dispersion (SD) techniques, with Neem Gum (NG) as a hydrophilic carrier. The effects of the polymer concentration and method of preparation on the solubility and dissolution rate were studied. The results showed that the solubility of ATR increases with increasing NG concentration. ( Rodde, Divase & Devkar,2014)

In 2015 a study showed that solubility of poorly water-soluble drugs is one of the most promising issue associated with these drugs to form a suitable dosage form that will provide desired pharmacological response. Results had shown that drug nature was changed from crystalline to amorphous and the complex was formed between drug and β-cyclodextrin. and had achieved maximum release of drug 97% within 45 min.

(Sarfraz, Ahmed and Mahmood,2015)

In 2015 a study showed that liquisolid systems (LSS) is a promising method for enhancing a dissolution rate and bioavailability of poorly soluble drugs. The release of the drug from LSS tablets is affected by many factors, including the disintegration time.

( Vranikivas ,2015)

In 2013 a research was done for the purpose of improving the solubility and dissolution rate of Atorvastatin, a drug belong to the group of statin by Solid Dispersion (SD) technique which was made by physical mixing and solvent evaporation method. Both method used a hydrophilic carrier Poloxamer 188 which was found to be played a vital role in the improvement of the dissolution property.

( Jahan, Islam and Tanwir ,2013)

In 2016 A research was done to develop an immediate release tablet formulation of Fenofibrate and Rosuvastatin in combination for better treatment as well as management of hypercholesterolemia and prevention of cardiovascular diseases.It was done in order to improve the dissolution profile of poorly soluble Fenofibrate.. The results showed that all tablets met the expected requirements for these tests and the release rate of fenofibrate also got improved giving an excellent dissolution profile for both fenofibrate and rosuvastatin.

( International journal of Pharmaceutical science and research , 2016)

In 2016 a research was done to enhance the solubility, dissolution rate, bioavailability of water insoluble drug pitavastatin by liquisolid technology and solid dispersions.It was found that liquisolid formulation tablets formulated with microcrystalline cellulose showed percentage drug release 63±2.42 at 5min and they showed significant higher drug release rates than pure drug

13±1.44 due to increase in wetting properties and surface of drug available for dissolution. FTIR spectral studies showed that there is no interaction between the drug and excipients.

( Mesa and Ampati, 2016)

At 2016, one study was done to develop a novel method for the fabrication of amorphous nano-solid dispersions of atorvastatin calcium, ezetimibe and atorvastatin and ezetimibe combination as poorly water soluble drugs. Here, electrospraying method was applied and it was proved to be an effiecient method for the fabrication of amorphous nano-solid dispersions of atorvastatin calcium, ezetimibe and atorvastatin and ezetimibe combination as poorly water soluble drugs.

( Jahangiri,Barzegar & Javadzadeh ,2016)

# CHAPTER THREE

# Materials

# &

# Method

# 3.1. Materials

## 3.1.1.Sample collection:

In order to observe the change in dissolution of Rosuvastatin with the presence of different supplements we collected 12 tablets of Rosuvastatin® (10mg) and 6 tablets of Calvimax D® (500mg) from local drug store in Dhaka as a sample.

**Table 3.1:Samples used in the experiment and theirsources**

| Sample Name | Source (supplier name) |
|---|---|
| **Ropiror® Tablet** | Opsonin Pharma |
| **Calvimax D® Tablet** | Incepta Pharmaceuticals Limited |

## 3.1.2.Reagents

We used distill water which was prepared in the laboratory of East West University.

## 3.1.3.Equipment & Instruments

**Table 3.2: List of Equipments used in the experiment**

| Serial No | Equipment | Source(Name of supplier) | Origin |
|---|---|---|---|
| 1 | UV-spectrophotometer | Shimadazu UV-1800 | Japan |
| 2 | Electronic balance | Precise XB120A | Switzerland |
| 3 | Dissolution tester | SMIC | China |
| 4 | Vernier caliper | China supplier | Shanghai, China |
| 5 | Hardness tester | Manually operated hardness tester | India |
| 6 | Distilled water plant | SMIC | China |

### 3.1.4. Apparatus

The apparatus are those were used throughout the experiments are listed in the following table

**Table 3.3: List of Apparatus**

| Serial No | Apparatus |
|---|---|
| 1 | **Beaker** |
| 2 | **Test tubes** |
| 3 | **Volumetric flasks (25ml , 50ml , 100ml )** |
| 4 | **Filter paper** |
| 5 | **Spatula** |
| 6 | **Glass rod** |
| 7 | **Syringe (5ml , 10ml)** |
| 8 | **Pipette pumper** |
| 9 | **Pipette ( 1ml , 2ml, 10ml )** |
| 10 | **Glass and Plastic funnel** |
| 11 | **Morter and Pastles** |

**Table 3.4: *In vitro* dissolution study**

| Dissolution medium | Distilled water |
|---|---|
| RPM | 50 |
| Time | 60 minutes |

Images of some important instruments those were used in different tests during research work

**Figure 3.1.:** Dissolution Tester(Tradeindia, 2016)

**Figure 3.2**: UV-1800 Double Beam Spectrophotometer(Tradeindia, 2016)

Images of some important instruments those were used in different tests during research work

**Figure 3.3.:** Electronic Balance(Tradeindia, 2016)

**Figure 3.4.:** Vernier caliper (Tradeindia, 2016)


Figure 3.5: Hardness tester (Tradeindia, 2016)

Figure 3.6: Distilled water apparatus (Tresnainstrument),

# 3.2. Methods

## Procedure

The release rate of Rosuvastatin tablet was determined by using tablet dissolution tester USPXXII. By using 900 ml water at pH 7.4 and at 37 degree Celsius and 50 RPM, the dissolution test was performed. At first 10 minutes and with the interval of 10 minutes sample of 10 ml was collected from the dissolution medium and the amount was replaced by 10 ml distill water. The sample was filtered through a Whatman filter paper. The absorbance of the solution was measured 241nm for Rosuvastatin drug by using a Shimadzu UV-1202 UV/ Visible double beam spectrophotometer. Percentage of drug release was calculated by using an equation which is obtained from standard curve. The dissolution was continued for 60 minutes to get stimulated picture of drug release in vivo condition and drug dissolve at specific time period was plotted as percent release versus time curve. (Shah et al. 1998)

## 3.2.1.Standard curve preparation

### 3.2.1.1.Preparation of dissolution medium for Standard Curve

Rasuvastatin is soluble in water. So distilled water was used as dissolution medium to make the standard curve. 500 ml of distilled water was prepared by using the distilled water propagating apparatus of East West University and that water was used to prepare the standard curve.

### 3.2.1.2.Preparation of Standard Curve

In order to prepare standard curve, at first different concentrations of rosuvastatin (0.001 mg/ml, 0.002 mg/ml, 0.003 mg/ml etc) were prepared. The following steps were followed to prepare these concentrations:

- Three Ropitor tablet were crushed in mortar and pestle.
- Equivalent weight of 10 mg of tablet was calipered and then it was dissolved in 100 ml of distilled water. According to this procedure the concentration of the stock solution became .01mg/ml.

- Then the solution in the volumetric flask was filtered and it was become the stock solution for the preparation of 0.001 mg/ml concentration.

## Calculations:

For the preparation of 0.001 mg/ml,

$V_1$= 0.001 mg/ml

$S_{1=}$ 15 ml

$S_2$= .01 mg/ml

$V_2$=?

We aginse that, $V_1 S_1 = V_2 S_2$

Or, $V_{2=} V_1 S_1 / S_2$

$V_{2=}$ [(0.001×15)/.01] ml

$V_2$= 1.5 ml

This 1.5 ml of stock solution was added with 13.5 ml of distilled water to obtain 15 ml of solution. The same calculation was followed for the preparation of 0.002 mg/ml, 0.003 mg/ml, 0.004 mg/ml, 0.005 mg/ml, 0.006 mg/ml, 0.007 mg/ml, 0.008 mg/ml and 0.009 mg/ml.

For,

- 0.002 mg/ml, 3 ml of stock solution was added with 12 ml of distilled water.
- 0.003 mg/ml, 4.5 ml of stock solution was added with 10 ml of distilled water.
- 0.004 mg/ml, 6 ml of stock solution was added with 9 ml of distilled water.
- 0.005 mg/ml, 7.5 ml of stock solution was added with 7.5 ml of distilled water.
- 0.006 mg/ml, 9 ml of stock solution was added with 6 ml of distilled water.
- 0.007 mg/ml, 10.5 ml of stock solution was added with 4.5 ml of distilled water.
- 0.008 mg/ml, 12 ml of stock solution was added with 3 ml of distilled water.
- 0.009 mg/ml, 13.5 ml of stock solution was added with 1.5 ml of distilled water.

**Table 3.5.: Prepared Concentration of Rosuvastatin**

| Serial no. | Concentration of Rosuvastatin (mg/ml) |
|---|---|
| **1** | 0.001 |
| **2** | 0.002 |
| **3** | 0.003 |
| **4** | 0.004 |
| **5** | 0.005 |
| **6** | 0.006 |
| **7** | 0.007 |
| **8** | 0.008 |
| **9** | 0.009 |

- Afterwards preparing the desired concentrations, the spectrophotometer was turned on and 241nm wavelength was set up as 241 nm was to be determined for showing the accurate result.
- The spectrophotometer was adjusted for 0 and 100% transmittance (T).
- The absorbances of the prepared solutions were measured later on.
- Then the absorbences were plotted against concentrations and a straight line was observed.

## 3.2.2.3. Preparation for dissolution test

### Preparation of dissolution medium

Distilled water was prepared in the laboratory and was used as dissolution medium for dissolution test. For each batch 6L of distilled water was prepared.

### 3.2.2.4.Method for dissolution test of Ropitor®(Rosuvastatin)

1. 6L (6000ml) of distilled water (dissolution medium) was prepared.

2. Each vessel of dissolution tester was filled with 900 ml of distilled water.
3. Time 1 hour, rpm 50 was set up in the dissolution machine.
4. Then the machine was allowed to warm up until it reached at 37.5 degree C.
5. Then 1 Ropitor® tablet was placed in every vessel.
6. After 10, 20,30, 40, 50 and 60 minutes 10 ml of solution was collected from each vessels and filtered, then from that 1 ml of solution was taken in another test tube and 9 ml distilled water was added to make it 10 ml.
7. At last UV absorbance off the solutions were taken where the wave length was 241.

**3.2.2.5.Method for dissolution test of Ropitor® (Rosuvastatin) with Calvimax D (Calcium supplement)**

1. 6L (6000ml) of distilled water (dissolution medium) was prepared.
2. Each vessel of dissolution tester was filled with 900 ml of distilled water.
3. Time 1 hour, rpm 50 was set up in the dissolution machine.
4. Then the machine was allowed to warm up until it reached at 37.5 degree C.
5. Then 1 Ropitor® tablet and 1 Calvimax D was placed in every vessel.
6. After 10, 20,30, 40, 50 and 60 minutes 10 ml of solution was collected from each vessels and filtered, then from that 1 ml of solution was taken in another test tube and 9 ml distilled water was added to make it 10 ml.
7. At last UV absorbance off the solutions were taken where the wave length was 241.

### 3.2.2.6.Determination of physical parameters

### 3.2.2.7.Weight Variation Test

**Procedure:**

1.10 tablets were taken and weighed.
2.The average was taken and it was considered as the standard weight of an individual tablet.
3.All tablets were weighed individually and observed whether the individual tablets are within the range or not.

N.B: The variation from the average weight in the weights not more than two tablets must not differ more than the percentage listed below.

**Table 3.6: Accepted percentage list for weight variation test of tablets**

| Weight of tablets | Percentage difference |
|---|---|
| 130 mg or less | ±10% |
| More than 130 to 324 mg | ±7.5% |
| More than 324 mg | ±5% |

**Equation:**

Following equation was used to determine % weight variation of tablets

$$\% \text{ Weight Variation} = (A\text{-}I/I) \times 100$$

Where,

Initial Weight of Tablet, I (gm)
Average weight of Tablets, A (gm)

### 3.2.2.8.Thickness test

**Procedure**

1.First the tablet was placed between the two jaws of the Vernier caliper.

2.Then the main scale reading was taken.

3.Next Vernier scale reading was taken also.

4.The two readings were added together for multiplying with the Vernier constant 0.1Cm.

**Calculation**

Following formula was used to determine thickness of tablets.

**Thickness of the tablet = Reading of Cm scale + Reading of Vernier scale × Vernier constant (0.01) + Vernier error**

### 3.2.2.9.Hardness test

**Procedure**

1.The slide scale of hardness tester was made zero.

2.One tablet was placed vertically between the two jaws of the tester.

3.Force was applied with a screw thread and spring until tablet fractured.

4.Reading in $Kg/cm^2$ was taken from the sliding scale.

# CHAPTER FOUR

# Results

# 4.1. Result

## General Information

The rosuvastatin samples were subjected to assay and dissolution profile analysis under the optimum situations. The objective of the assay was to assess the samples for compliance with pharmacopeias limits for content.

## Physical parameters

## 4.1.1.Results from weight variation

**Table 4.1:Weight variation of Ropitor® tablets**

| Tablet No | Initial weight I (mg) | Average weight A (mg) | % Weight variation (A-I)/I *100 |
|---|---|---|---|
| 1 | 0.101 | | 2 |
| 2 | 0.103 | | -0.97 |
| 3 | 0.100 | | 2 |
| 4 | 0.102 | | 0 |
| 5 | 0.102 | 0.102 | 0 |
| 6 | 0.100 | | 2 |
| 7 | 0.103 | | -0.97 |
| 8 | 0.103 | | -0.97 |
| 9 | 0.106 | | -3.77 |
| 10 | 0.100 | | 2 |

### 4.1.2.Results from thickness

**Table 4.2: Thickness of Ropitor® Tablets**

| Tablet No | Main scale reading (cm), M | Vernier scale reading (cm), V | Thickness of the tablet (cm), (M+V) |
|---|---|---|---|
| 1 | 0.3 | 0.5 | 3.35 |
| 2 | 0.3 | 1 | 0.4 |
| 3 | 0.3 | 1 | 0.4 |
| 4 | 0.3 | 1 | 0.4 |
| 5 | 0.3 | 0.5 | 3.35 |
| 6 | 0.3 | 0.5 | 3.35 |
| 7 | 0.3 | 1 | 0.4 |
| 8 | 0.3 | 0.5 | 3.35 |
| 9 | 0.3 | 0.5 | 3.35 |
| 10 | 0.3 | 0.5 | 3.35 |

### 4.1.3.Results from Hardness tests

**Table 4.3: Hardness of Ropitor® Tablets.**

| Tablet No. | Hardness ($Kg/cm^2$) | Average |
|---|---|---|
| 1 | 2.45 | |
| 2 | 2.7 | |
| 3 | 2.6 | |
| 4 | 2.0 | |
| 5 | 2.5 | 2.35 |
| 6 | 2.4 | |
| 7 | 2.0 | |
| 8 | 1.9 | |
| 9 | 2.6 | |
| 10 | 2.4 | |

### 4.2.1. Standard Curve Preparation

**Table 4.4: Concentration and Absorbance for Standard curve of Rosuvastatin (Ropitor®).**

| Serial No. | Concentration(µg/ml) | Absorbance |
|---|---|---|
| 1 | 0 | 0. |
| 2 | 0.001 | 0.037 |
| 3 | 0.002 | 0.08 |
| 4 | 0.003 | 0.113 |
| 5 | 0.004 | 0.151 |
| 6 | 0.005 | 0.186 |
| 7 | 0.006 | 0.256 |
| 8 | 0.007 | 0.259 |
| 9 | 0.008 | 0.297 |
| 10 | 0.009 | 0.336 |

By plotting the concentration against the absorbance of Rosuvastatin we found a straight line. From the standard curve Rosuvastatin, we derived an equation y=37.59x+0.0023 & $R^2$=0.992(Here, y= Absorbance and x=Concentration of drug). We use this equation to get the concentration from different samples absorbance of Rosuvastatin.

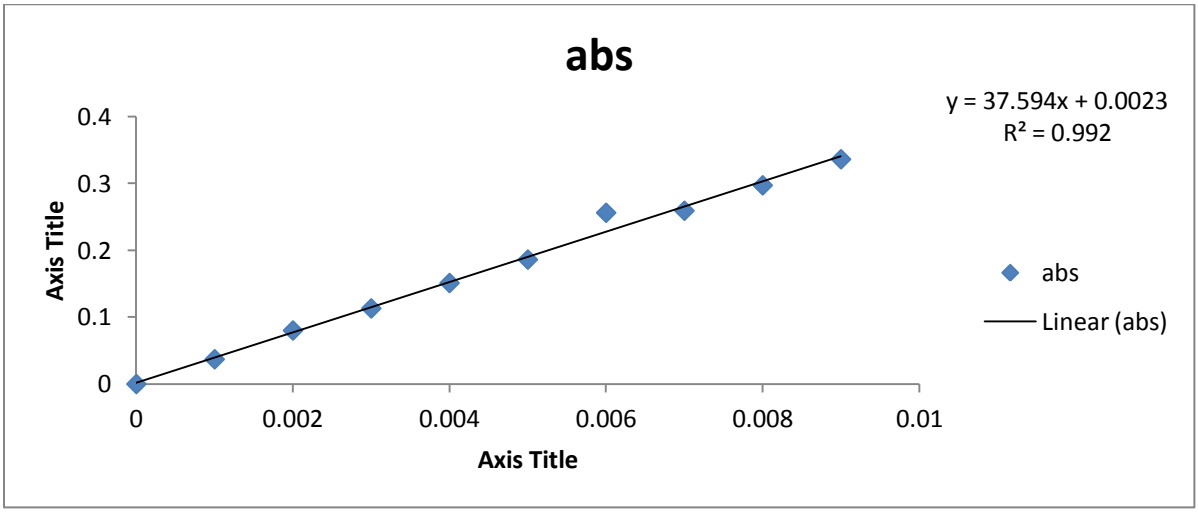


Figure 4.1:Graph showing straight line for absorbance with respect to concentration for Rosuvastatin

### 4.2.2.Results of the dissolution test of individual Ropitor®, Ropitor® without calcium supplement drugs Calvimax D ® and the impact of the supplement on the dissolution of Rosuvastatin® after 10 minute ,20 minute,30 minute, 40 minute,50 minute and 60 minute.

### Dissolution test of Ropitor® (Rosuvastatin) without any supplement

**Table 4.5: UV absorbance , dissolved amount and % release of only Ropitor® (Rosuvastatin) 10mg tablet after 10 ,20 and 30 minute**

| | After 10 minutes | | | After 20 minutes | | | After 30 minutes | | |
|---|---|---|---|---|---|---|---|---|---|
| Serial No. | Absorbance | Dissolved Amount (mg) | % Release | Absorbance | Dissolved Amount (mg) | % release | Absorbance | Dissolved Amount (mg) | % Release |
| 1 | 0.196 | 4.637 | 46.371 | 0.224 | 5.307 | 53.075 | 0.245 | 5.810 | 58.102 |
| 2 | 0.194 | 4.589 | 45.892 | 0.217 | 5.140 | 51.399 | 0.248 | 5.882 | 58.821 |
| 3 | 0.193 | 4.565 | 45.693 | 0.219 | 5.188 | 51.878 | 0.246 | 5.834 | 58.342 |
| 4 | 0.196 | 4.637 | 46.371 | 0.222 | 5.260 | 52.596 | 0.250 | 5.930 | 59.299 |
| 5 | 0.195 | 4.613 | 46.132 | 0.224 | 5.307 | 53.075 | 0.248 | 5.882 | 58.821 |
| 6 | 0.194 | 4.589 | 45.892 | 0.223 | 5.284 | 52.836 | 0.247 | 5.858 | 58.581 |

**Table 4.6: UV absorbance , dissolved amount and % release of only Ropitor® (Rosuvastatin) 10mg tablet after 40 ,50 and 60 minute**

| | After 40 minutes | | | After 50 minutes | | | After 60 minutes | | |
|---|---|---|---|---|---|---|---|---|---|
| Serial No. | Absorbance | Dissolved Amount (mg) | % Release | Absorbance | Dissolved Amount (mg) | % release | Absorbance | Dissolved Amount (mg) | % Release |
| 1 | 0.258 | 6.121 | 61.215 | 0.279 | 6.624 | 66.242 | 0.299 | 7.103 | 71.030 |
| 2 | 0.259 | 6.145 | 61.454 | 0.278 | 6.600 | 66.003 | 0.307 | 7.295 | 72.945 |
| 3 | 0.260 | 6.169 | 61.693 | 0.275 | 6.528 | 65.284 | 0.297 | 7.055 | 70.551 |
| 4 | 0.258 | 6.121 | 61.215 | 0.279 | 6.624 | 66.242 | 0.299 | 7.103 | 71.030 |
| 5 | 0.259 | 6.145 | 61.454 | 0.278 | 6.600 | 66.003 | 0.303 | 7.199 | 71.988 |
| 6 | 0.257 | 6.107 | 61.071 | 0.277 | 6.576 | 65.763 | 0.301 | 7.151 | 71.509 |

#### 4.2.2.1.Calculation of dissolved amount for Ropitor®(Rosuvastatin)

From the standard curve an equation was found which was,Y= 37.594x+0.0023

Here, Y= Absorbance X=concentration=?

Dilution factor=9000

When the absorbance was 0.201, the following equation can be written as

0.201=37.594x+0.0023

37.594x= 0.201-0.0023

37.594x = 0.1987

X= 0.1987/37.594

X=0.00528

So, Dissolve amount of Ropitor®(Rosuvastatin) was =0.00528*900=4.756

#### 4.2.2.2.Calculation of % release for Ropitor®(Rosuvastatin)

% release = dissolved amount*100/10

For dissolved amount 4.756

% release = 4.756*100/10

=47.56 %

By putting the other absorbance values in the same equation different dissolved amounts of Ropitor®(Rosuvastatin) was calculated.

**4.3.Table 4.7: UV absorbance , dissolved amount and % release of only Ropitor® (Rosuvastatin) 10mg tablet with Calvimax D ( Calcium supplement) after 10 ,20 and 30 minute**

| | **After 10 minutes** | | | **After 20 minutes** | | | **After 30 minutes** | | |
|---|---|---|---|---|---|---|---|---|---|
| Serial No. | Absorbance | Dissolved Amount (mg) | % Release | Absorbance | Dissolved Amount (mg) | % release | Absorbance | Dissolved Amount (mg) | % Release |
| 1 | 0.161 | 3.799 | 37.992 | 0.185 | 4.374 | 43.738 | 0.198 | 4.685 | 46.851 |
| 2 | 0.163 | 3.847 | 38.471 | 0.186 | 4.398 | 43.978 | 0.196 | 4.637 | 46.372 |
| 3 | 0.161 | 3.799 | 37.992 | 0.187 | 4.422 | 44.217 | 0.199 | 4.709 | 47.090 |
| 4 | 0.163 | 3.847 | 38.471 | 0.188 | 4.446 | 44.457 | 0.197 | 4.661 | 46.611 |
| 5 | 0.162 | 3.823 | 38.232 | 0.189 | 4.470 | 44.696 | 0.199 | 4.709 | 47.090 |
| 6 | 0.160 | 3.775 | 37.753 | 0.185 | 4.374 | 43.738 | 0.198 | 4.685 | 46.851 |

**Table 4.8: UV absorbance , dissolved amount and % release of only Ropitor®(Rosuvastatin) 10mg tablet with Calvimax D ( Calcium supplement) after 40 ,50 and 60 minute**

| | **After 40 minutes** | | | **After 50 minutes** | | | **After 60 minutes** | | |
|---|---|---|---|---|---|---|---|---|---|
| Serial No. | Absorbance | Dissolved Amount (mg) | % Release | Absorbance | Dissolved Amount (mg) | % release | Absorbance | Dissolved Amount (mg) | % Release |
| 1 | 0.212 | 5.020 | 50.202 | 0.239 | 5.667 | 56.660 | 0.258 | 6.121 | 61.215 |
| 2 | 0.216 | 5.116 | 51.160 | 0.232 | 5.499 | 54.990 | 0.255 | 6.050 | 60.496 |
| 3 | 0.217 | 5.140 | 51.399 | 0.236 | 5.595 | 55.948 | 0.226 | 6.074 | 60.736 |
| 4 | 0.217 | 5.140 | 51.399 | 0.234 | 5.547 | 55.469 | 0.259 | 6.145 | 61.454 |
| 5 | 0.219 | 5.188 | 51.878 | 0.236 | 5.595 | 55.948 | 0.257 | 6.098 | 60.975 |
| 6 | 0.212 | 5.020 | 50.202 | 0.240 | 5.691 | 56.905 | 0.258 | 6.121 | 61.215 |

Calculation for dissolved amount (mg) of Ropitor®(Rosuvastatin) with Calvimax D (Calcium supplement).

By using,Y=37.594x+0.0023 equation dissolved amount of Ropitor®(Rosuvastatin) with Calvimax D (Calcium supplement) was calculated.

**4.4.Impact of Calcium & Vitamin D suppliment on the dissolution of Ropitor after 10 minutes.**

**Table 4.9: Percentage calculation for dissolved amount of Ropitor®(Rasuvastatin), Ropitor®Rosuvastatin)with Calvimax D (Calcium supplement) and the impact of Calvimax D on the dissolution of Ropitor®(Rasuvastatin) of after 10 minutes**

| **Ropitor® without any supplement** | | | | **Ropitor® with Calvimax D** | | | | |
|---|---|---|---|---|---|---|---|---|
| Dissolved amount (mg) | Average dissolved amount (mg) | Percent dissolved amount (%) | Average percent dissolved amount (% | Dissolved amount (mg) | Average dissolved amount (mg) | Percent dissolved amount (%) | Average percent dissolved amount (%) | impact on dissolution (%) |
| 4.63 | | 46.37 | | 3.79 | | 37.99 | | |
| 4.58 | | 45.89 | | 3.84 | | 38.47 | | |
| 4.56 | 4.59 | 45.65 | 46.05 | 3.79 | 3.80 | 37.99 | 38.08 | -17.30 |
| 4.63 | | 46.37 | | 3.84 | | 38.47 | | |
| 4.61 | | 46.13 | | 3.82 | | 38.23 | | |
| 4.58 | | 45.89 | | 3.77 | | 37.75 | | |

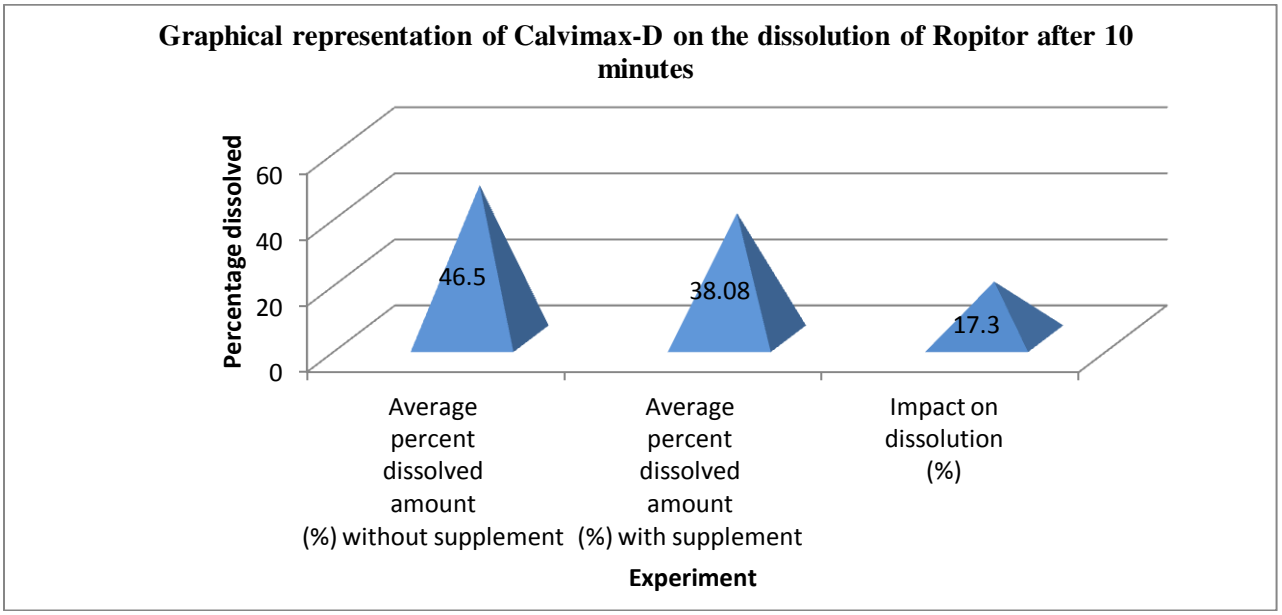


**Figure 4.2:** Graphical representation of Calvimax-D on the dissolution of Ropitor®

### 4.5.Impact of Calcium & Vitamin D suppliment on the dissolution of Ropitor after 20 minutes.

**Table 4.10: Percentage calculation for dissolved amount of Ropitor®(Rosuvastatin), Ropitor®(Rosuvastatin)with Calvimax D 500 (Calcium supplement) and the impact of Calvimax D on the dissolution of Ropitor®(Rosuvastatin) after 20 minutes**

| Ropitor® without any supplement | | | | Ropitor® with Calvimax D | | | | |
|---|---|---|---|---|---|---|---|---|
| Dissolved amount (mg) | Average dissolved amount (mg) | Percent dissolved amount (%) | Average percent dissolved amount (%) | Dissolved amount (mg) | Average dissolved amount (mg) | Percent dissolved amount (%) | Average percent dissolved amount (%) | impact on dissolution (%) |
| 5.30 | | 53.07 | | 4.37 | | 43.73 | | |
| 5.14 | | 51.39 | | 4.39 | | 43.98 | | |
| 5.18 | 5.24 | 51.87 | 52.47 | 4.42 | 4.41 | 44.21 | 44.13 | -15.89 |
| 5.26 | | 52.59 | | 4.44 | | 44.45 | | |
| 5.30 | | 53.07 | | 4.47 | | 44.69 | | |
| 5.28 | | 52.83 | | 4.37 | | 43.73 | | |

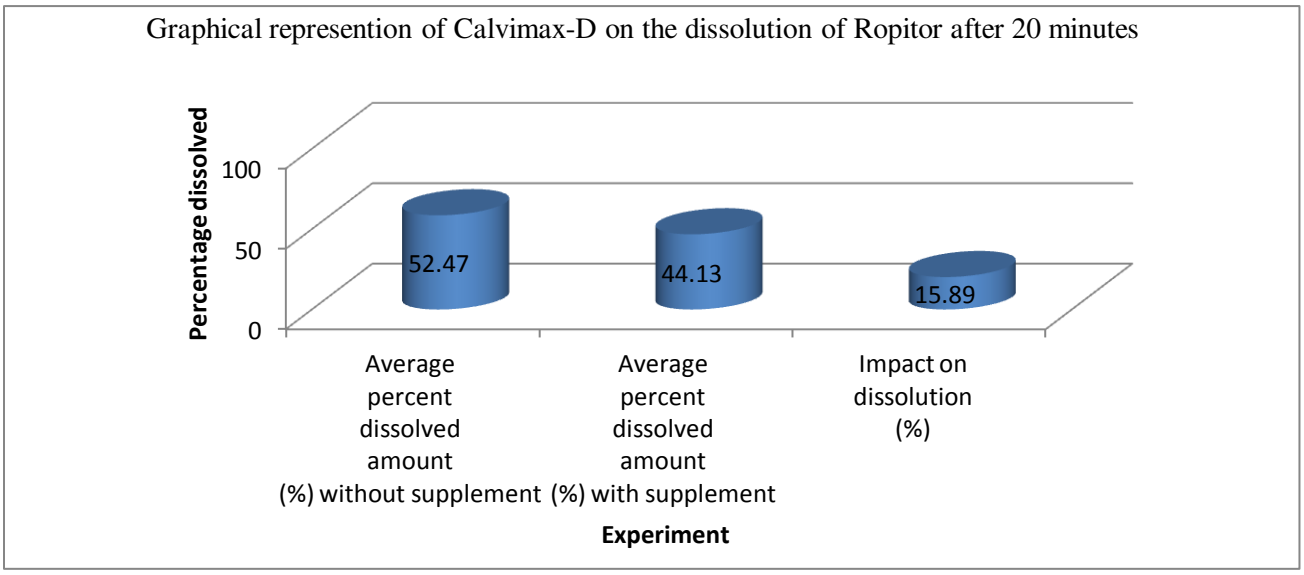


**Figure 4.3:** Graphical representation of Calvimax-D on the dissolution of Ropitor®

**4.6.Impact of Calcium & Vitamin D suppliment on the dissolution of Ropitor after 30minutes.**

**Table 4.11: Percentage calculation for dissolved amount of Ropitor®(Rosuvastatin), Ropitor®(Rosuvastatin)with Calvimax D (Calcium supplement) and the impact of Calvimax D on the dissolution of Ropitor®(Rosuvastatin) after 30 minutes**

| **Ropitor® without any supplement** | | | | **Ropitor® with Calvimax D** | | | | |
|---|---|---|---|---|---|---|---|---|
| Dissolved amount (mg) | Average dissolved amount (mg) | Percent dissolved amount (%) | Average percent dissolved amount (% | Dissolved amount (mg) | Average dissolved amount (mg) | Percent dissolved amount (%) | Average percent dissolved amount (%) | impact on dissolution (%) |
| 5.81 | | 58.10 | | 4.68 | | 46.85 | | |
| 5.88 | | 58.82 | | 4.63 | | 46.37 | | |
| 5.83 | 5.66 | 58.34 | 58.65 | 4.70 | 4.67 | 47.09 | 46.81 | -20.18 |
| 5.93 | | 59.29 | | 4.66 | | 46.61 | | |
| 5.88 | | 58.82 | | 4.70 | | 47.09 | | |
| 5.85 | | 58.58 | | 4.68 | | 46.85 | | |

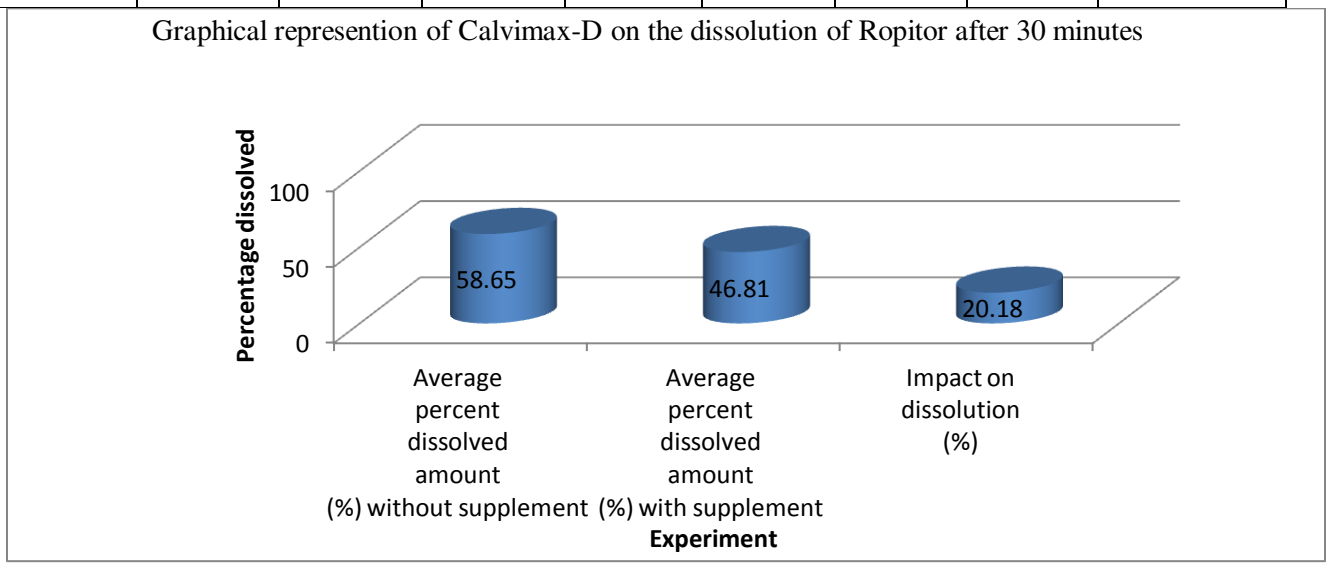


**Figure 4.4:** Graphical representation of Calvimax-D on the dissolution of Ropitor®

### 4.7.Impact of Calcium & Vitamin D suppliment on the dissolution of Ropitor after 40 minutes.

**Table 4.12: Percentage calculation for dissolved amount of Ropitor® (Rosuvastatin), Ropitor®(Rosuvastatin)with Calvimax D 500 (Calcium supplement) and the impact of Calvimax D on the dissolution of Ropitor® (Rosuvastatin) after 40 minutes**

| Ropitor® without any supplement | | | | Ropitor® with Calvimax D | | | | |
|---|---|---|---|---|---|---|---|---|
| Dissolved amount (mg) | Average dissolved amount (mg) | Percent dissolved amount (%) | Average percent dissolved amount (% | Dissolved amount (mg) | Average dissolved amount (mg) | Percent dissolved amount (%) | Average percent dissolved amount (%) | impact on dissolution (%) |
| 6.12 | | 61.21 | | 5.02 | | 50.20 | | |
| 6.14 | | 61.45 | | 5.11 | | 51.16 | | |
| 6.16 | 6.13 | 61.69 | 61.34 | 5.14 | 5.10 | 51.39 | 51.03 | -16.80 |
| 6.12 | | 61.21 | | 5.14 | | 51.39 | | |
| 6.14 | | 61.45 | | 5.18 | | 51.87 | | |
| 6.10 | | 61.07 | | 5.02 | | 50.20 | | |

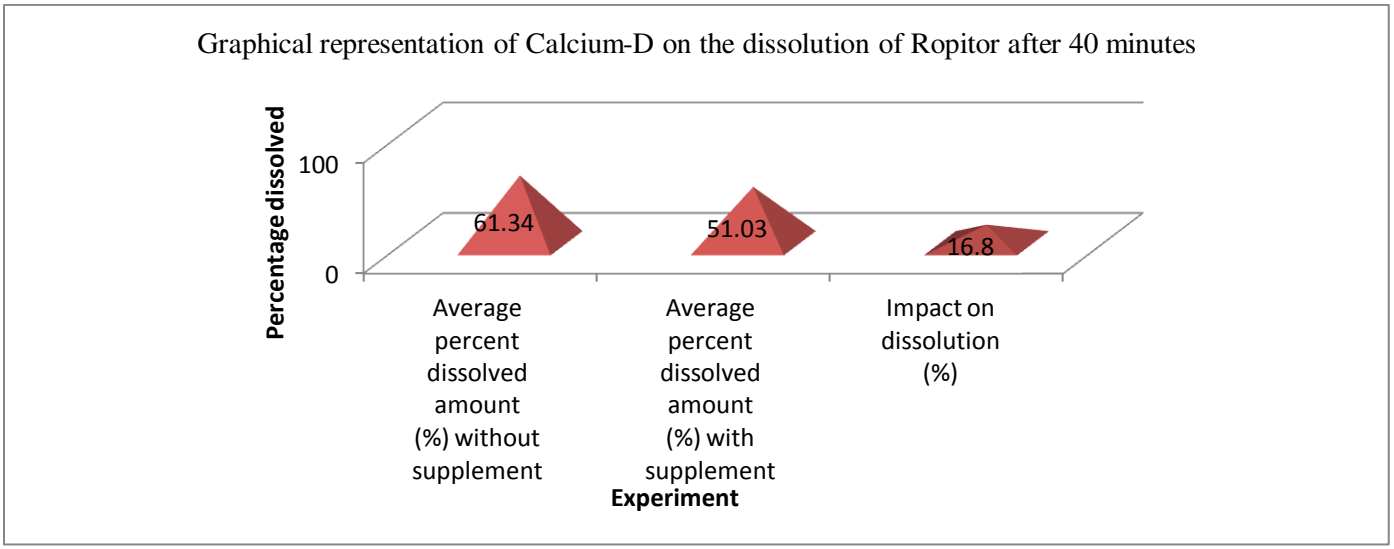


**Figure 4.5:** Graphical representation of Calvimax-D on the dissolution of Ropitor®

**4.8.Impact of Calcium & Vitamin D suppliment on the dissolution of Ropitor after 50 minutes.**

**Table 4.13: Percentage calculation for dissolved amount of Ropitor®(Rosuvastatin), Ropitor®(Rosuvastatin)with Calvimax D (Calcium supplement) and the impact of Calvimax D on the dissolution of Ropitor®(Rosuvastatin) after 50 minutes**

| **Ropitor® without any supplement** | | | | **Ropitor® with Calvimax D** | | | | |
|---|---|---|---|---|---|---|---|---|
| Dissolved amount (mg) | Average dissolved amount (mg) | Percent dissolved amount (%) | Average percent dissolved amount (% | Dissolved amount (mg) | Average dissolved amount (mg) | Percent dissolved amount (%) | Average percent dissolved amount (%) | impact on dissolution (%) |
| 6.62 | | 66.24 | | 5.66 | | 56.66 | | |
| 6.60 | | 66.00 | | 5.49 | | 54.99 | | |
| 6.52 | 6.48 | 65.28 | 65.92 | 5.59 | 5.59 | 55.94 | 55.98 | -15.07 |
| 6.62 | | 66.24 | | 5.547\ | | 55.46 | | |
| 6.60 | | 66.00 | | 5.59 | | 55.94 | | |
| 6.57 | | 65.76 | | 5.69 | | 56.90 | | |

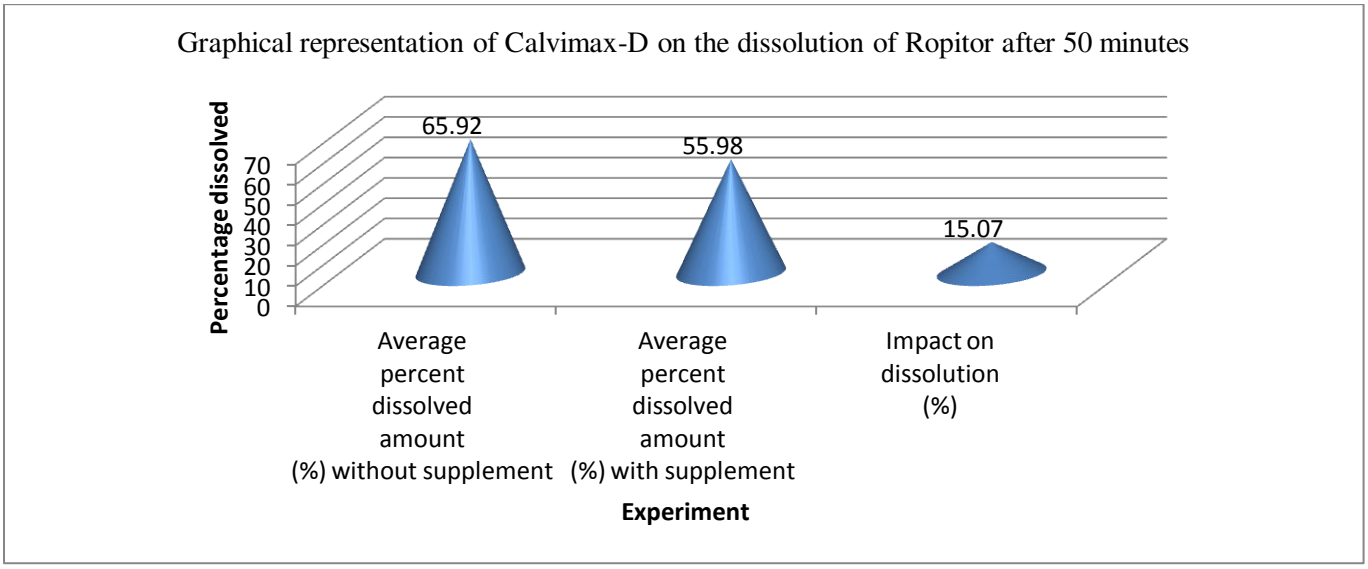


**Figure 4.6:** Graphical representation of Calvimax-D on the dissolution of Ropitor®

**4.9.Impact of Calcium & Vitamin D suppliment on the dissolution of Ropitor after 60 minutes**.

**Table 4.14: Percentage calculation for dissolved amount of Ropitor®(Rasuvastatin), Ropitor®(Rosuvastatin)with Calvimax D 500 (Calcium supplement) and the impact of Calvimax D on the dissolution of Ropitor®(Rosuvastatin) after 60 minutes**

| **Ropitor® without any supplement** | | | | **Ropitor® with Calvimax D** | | | | |
|---|---|---|---|---|---|---|---|---|
| Dissolved amount (mg) | Average dissolved amount (mg) | Percent dissolved amount (%) | Average percent dissolved amount (% | Dissolved amount (mg) | Average dissolved amount (mg) | Percent dissolved amount (%) | Average percent dissolved amount (%) | impact on dissolution (%) |
| 7.10 | | 71.03 | | 6.12 | | 61.21 | | |
| 7.29 | | 72.94 | | 6.05 | | 60.49 | | |
| 7.05 | 7.14 | 70.55 | 71.46 | 6.07 | 6.09 | 60.73 | 61.01 | -14.62 |
| 7.10 | | 71.03 | | 6.14 | | 61.45 | | |
| 7.19 | | 71.988 | | 6.09 | | 60.97 | | |
| 7.15 | | 71.50 | | 6.12 | | 61.21 | | |
| | | | | | | | | |

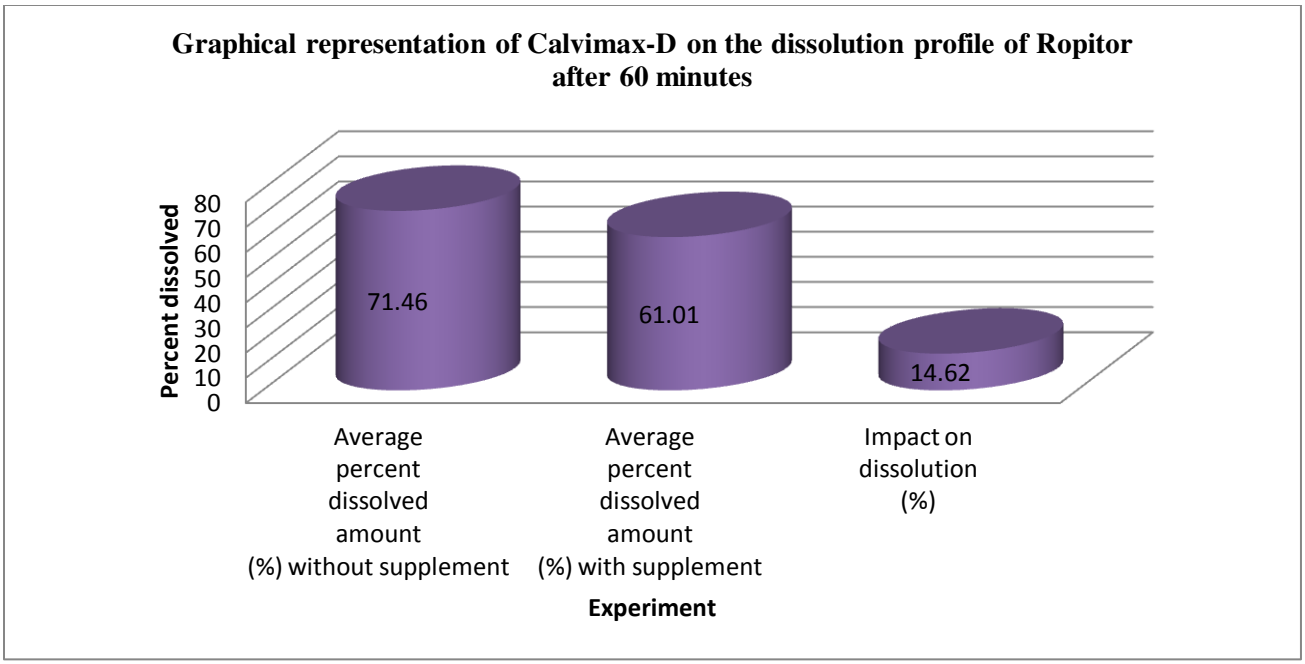


**Figure 4.7:** Graphical representation of Calvimax-D on the dissolution of Ropitor®

**4.10.Impact of of Ropitor®(Rasuvastatin), Ropitor®(Rosuvastatin)with Calvimax D(Calcium supplement) after 10, 20, 30, 40 ,50 and 60 minutes**

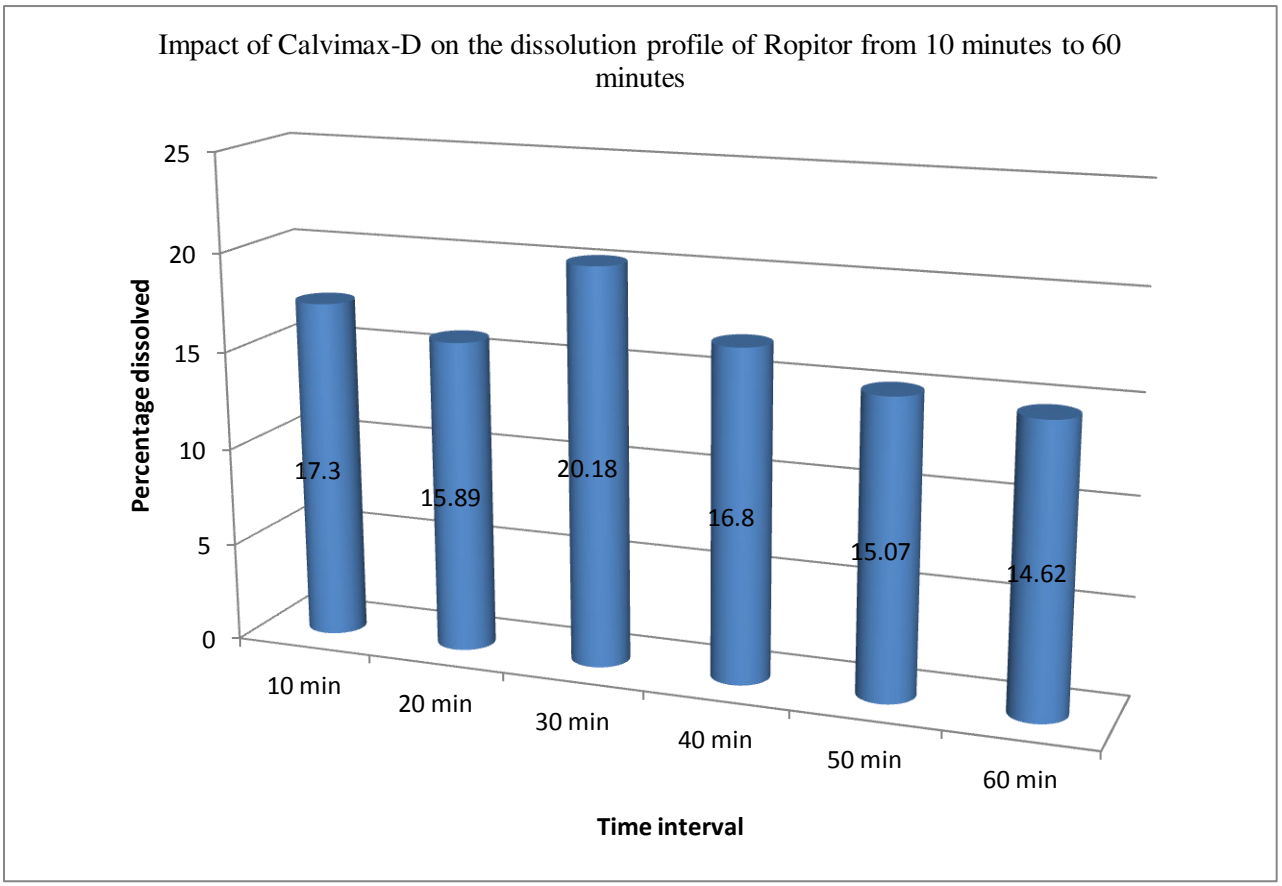


Figure 4.8: Graphical representation of gradual change of impact Ropitor®(Rosuvastatin)with Calvimax D

# CHAPTER FIVE
# Discussion

## 5.1. Discussion

Weight variation of sample tablets Ropitor® indicated the uniformity of the solid dosage forms. USP provides an accepted percentage for weight variation test and our products were within that range. The hardness of the tablets are slightly increased with the increase in weight content without much variation in content uniformity of weight. Weight variation test indicates the good manufacturing practice(GMP), appropriate size of the tablets and the content uniformity of the formulation. (Nasrin et al.,2011).

The thickness of all tablets Ropitor® were determined by vernier calipers and all values were close. Thickness determination was important because it relates with tablet hardness. If the thickness of a tablet is materially changed, then all tablet hardness comparisons will become incorrect (Pitt and Heasley, 2013).

Hardness determination is important because the dissolution of a drug product depends on its hardness. The hardness increase caused by higher compression loads in the absence of a moisture-induced effect, which is responsible for decrease in the invitro dissolution as the hardness was increased (Chowhan and Palagyi, 1978).

If the tablet is too hard, it may not disintegrate in the required period of time to meet the dissolution specifications. (Nasrin et al.,2011).

From the result of dissolution tests of Ropitor®, it was observed that the percent release of drug for Rosutin® was increasing with time. After 10 minutes, 20 minutes,30 minutes, 40 minutes,50 minutes and 60 minutes, the average percent release of drug were 46.05%, 52.47% , 58.65%, 61.34% ,65.92% and 71.46% respectively. So, it was observed that the release of drug is increasing gradually with increasing time.

When Ropitor® was incorporated with Calvimax- D (calcium-vitamin D supplement), the dissolution was altereded. After 10 minutes, 20 minutes,30 minutes, 40 minutes,50 minutes and 60 minutes, the average percent release of drug were 38.08%, 44.13%, 46.81%, 51.03%, 55.98% and 61.01% respectively. So, it was demonstrated that with increasing time the dissolution or the drug release of Ropitor® is decreased when it is combined with calcium and vitamin D

supplement.At 10 minutes it created an Impact of 17.30% and after 60 minutes the impact changed into 14.62%.

This release of drug is decreased due to the common ion effect. The solubility decreases when a soluble or weakly soluble compound is combined with its ionic part.

When Calvimax-D (Calium and vitamin D) was given with Ropitor® (Rosuvastatin Ca), solubility was decreased and it was due to common ion effect . According to the Le Chatelier's principle,if the concentration of any ion increases in the solution, then the equilibrium of the solution is shifted to the left to make a balance between free ion and bound ion. So addition of Calvimax-D ( Calium and vitamin D) reduced the solubility which also decreased the dissolution rate.

Finally, it can be said that Ropitor® and Calvimax-D should not be co-administered. There should be a minimum time interval for administering these two drugs.

# CHAPTER SIX
# Conclusion

## 6.1 Conclusion

In the study, significant differences were observed in the dissolution profiles of the rosuvastatin products tested. The results obtained from this study can be extrapolated to the wider Bangladesh market. The city harbours many pharmaceutical manufacturing industries and acts as a centre of distribution for imported drugs. In addition, the sub-counties in Dhaka focus the economic capacities of the Bangladesh population, which in turn affects stocking patterns for the drug products. A significant percentage of generic products in the market may not be pharmaceutically equivalent to their innovator counterparts. As such, results of clinical studies conducted on the innovator product may not necessarily be applicable to generic products. Consequently, the generic products in the Bangladesh market may not be interchangeable with the innovator product and their efficacy may also not be comparable to that of innovator drugs.

# CHAPTER SEVEN

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